

Remarks

As an initial matter, Applicants inform the Office that their patent prosecution counsel has changed to Fulbright & Jaworski L.L.P. Please note the new contact information listed under the signature block.

A. *Status of Claims*

Claims 14, 15, 17–26, and 28–29 were pending. Claims 16 and 27 were withdrawn in view of a species election requirement. Claims 14, 15, and 18– 24 are amended in this response. Claims 17, 25–26 and 28–29 are canceled. Claims 30–46 are added. Claims 14, 15, 18–24, and 30–46 are now pending. No new matter has been added.

For the Examiner’s convenience, a clean version of the pending claims (reflecting the amendments made here) is included as Appendix A.

B. *Status of Specification*

The specification has been amended to clarify the priority-tree of the current application. The parent of this application indicated that it was a continuation-in-part (“CIP”) of U.S. Serial No. 08,627,843, which was a non-provisional of U.S. Serial No. 60/004,906. However, the parent of this application forgot to mention that U.S. Serial No. 08,627,843 is *also* a CIP of U.S. Serial No. 08,402,145 (*see* “Related U.S. Application Data” of U.S. Patent No. 6,074,605 for confirmation). The amendment presented here corrects that oversight. The specification has also been amended to reference issued patent numbers where appropriate.

C. *Species Restriction*

Applicants acknowledge the election of species made earlier and the withdrawal of claims 16 and 27 as drawn to non-elected species.

D. All the Claims Satisfy the Written Description Requirement

Claims 20 and 22–24 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking written description. Applicants respectfully traverse.

Claim 20 was rejected for its use of the phrase “mechanisms for breaking . . .” No *prima facie* case of lack-of-written-description has been established. Nevertheless, Applicants have chosen to amend claim 20 to recite “means for breaking . . .” This means-plus-function language is explicitly contemplated by 35 U.S.C. § 112, 6th paragraph and is proper. Removal of this rejection is respectfully requested.

Claims 22–24 stand rejected for their use of the phrase “controller.” Applicants respectfully traverse. The Examiner asserts, without *any* supporting evidence, that a “controller” is “not adequately described in the specification” and is “not conventional in the art.” *See* Office Action, p. 3. The Examiner also asserts, without *any* supporting evidence, that “a skilled artisan cannot envision the detailed structure of a genus of the . . . controllers,” in another attempt to justify the rejection. *See* Office Action, p. 4. It appears that the Examiner has cut-and-paste portions of a written description, genus-based rejection from a chemical or biotech case into the present action. *See* Office Action, p. 3 (bottom) (stating, “It is not sufficient to support the present claimed invention directed to functional languages because the disclosure of no more than species inert polymers as the first co-dispersant compound as in the instant case . . .”). This cut-and-paste argument does not fit the present facts.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. MPEP. § 2163 (citing *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991). Here, the specification describes computerized

equipment for controlling, for instance, pumps and other components of the invention. Thus, there is adequate support for claiming a “controller” (which is a very familiar computer term with a well-understood meaning supported by the disclosure) associated with, *e.g.*, a pump.

Nevertheless, in an attempt to simplify and clarify claim language, independent claim 22 has been amended to recite “computer” instead of “controller.” Applicants believe that this non-substantive amendment clarifies the claim due at least to the familiarity of the phrase “computer” to those of ordinary skill in the art. No reasonable argument can be made that written description is lacking for this phrase, as it is used in amended claim 22. For instance, the Examiner is directed at least to page 61, lines 1–4, which describes that the pump can operate under control of a *computer* algorithm. For even further support for computer embodiments, the Examiner is directed to page 63, lines 4–23, which describes that the pump can also be controlled by circuit board computation means. Because such description clearly and explicitly supports the present claims, the written description is satisfied, and Applicants respectfully request that this rejection be withdrawn.

E. All the Claims Are Enabled

Claims 20 and 22–24 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. Applicants respectfully traverse.

With respect to claim 20, the Examiner argues that enablement is only present for a particular phrase (suggested by the Examiner) because written description is lacking for anything else. This position is faulty and squarely contradicts the law. *See MPEP § 2164* (explaining that the enablement and written description requirements are separate and that a lack of written description does not necessarily mean that enablement is lacking). Further, *no* evidence is provided to support the lack-of-enablement allegation, so no *prima facie* case is established.

Nevertheless, as mentioned above, claim 20 has been amended to conform to the classic means-plus-function format. The claim now recites “means for breaking,” and the specification provides several structural possibilities (and equivalents) to achieve the recited function of “breaking.” For example, the Examiner is directed at least to Figure 20 and its accompanying text. No reasonable argument can be presented to suggest that, despite such description and detailed mechanical (*i.e.* a predictable art) drawing, claim 20 is not-enabled. Rather, claim 20 and its dependent claim 21 clearly meet the requirements of 35 U.S.C. § 112, and the current rejection should be withdrawn.

With respect to claim 22, the Examiner raises similar arguments—support only exists for the phrase “circuit board,” and nothing else is enabled. Again, this type of argument explicitly contradicts the guidelines and law surrounding enablement. *See MPEP § 2164.*

A correct framework for an enablement analysis involves the following considerations. “The specification must teach those skilled in the art how to make and use the full scope of the claimed invention without ‘undue experimentation.’” *See MPEP § 2164.08* (citing *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993)). “As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied.” *See MPEP § 2164.01(b)* (citing *In re Fisher*, 427 F.2d 833, 839 (CCPA 1970)).

Applicants respectfully note that “it is *incumbent* upon the Patent Office ... to explain why it doubts the truth or accuracy of any statement in a supporting disclosure *and to back up assertions of its own with acceptable evidence or reasoning* which is inconsistent with the contested statement.” *See MPEP § 2164.04* (quoting *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971)). For example, the court in *Gould v. Mossinghoff*, 229 USPQ 1 (D.C. 1985) stated:

In examining a patent application, the PTO is required to assume that the specification complies with the enablement provisions of Section 112 unless it has “acceptable evidence or reasoning” to suggest otherwise. *In re Marzocchi*, 439 F.2d 220, 223-24, 169 USPQ 367, 369-370 (CCPA. 1971).

The PTO thus must provide reasons supported by the record as a whole what the specification is not enabling. *Application of Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219-220 (CCPA 1979). Then and only then does the burden shift to the applicant to show that one of ordinary skill in the art could have practiced the claimed invention without undue experimentation. *In re Strahilevitz*, 668 F.2d. 1229, 1232, 212 USPQ 561, 563-64 (CCPA 1982). (Emphasis added.)

“The enablement requirement is met if the description enables *any* mode of making and using the invention.” *Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 1361 (Fed. Cir. 1998) (quoting *Engel Indus. Inc. v. Lockformer Co.*, 946 F.2d 1528, 1533 (Fed. Cir. 1991)).

Here, the specification describes computer-controllable pumps and other components. See specification, page 61, lines 1–4; page 63, lines 4–23. The Examiner has not, and cannot given such description, bring forth evidence that the claims are not enabled due to the recitation of a “computer.” Accordingly, the current rejection should be withdrawn.

F. All the Claims Are Patentable Over Nicolau

Claims 22–26 and 28–29 stand rejected as being anticipated or rendered obvious by WO 94/2117 (“Nicolau”). Applicants respectfully traverse.

Nicolau is cited in the specification as being a “related” application. See specification p. 26, lines 18–21. Nicolau, in fact, shares several of the same figures as the present application. However, the present claims have been drafted to ensure that Nicolau does not disclose or suggest the inventions of those claims, including rejected claims 22–26 and 28–29.

In particular, the present claims are directed to embodiments generally illustrated at figures 14 and subsequent. Those figures, and their accompanying text, are totally absent from Nicolau. Specifically, Nicolau fails to disclose or even suggest the:

- “computer-controllable pump in fluid communication with the fluid flow path and configured to establish a flow rate of the fluid flow path in accordance with a sample processing rate” of amended claim 14;
- “means for breaking the electrodes prior to the apparatus being removed from the support member whereby the apparatus cannot be re-used” of amended claim 20;
- “computer responsive to the rate at which the pump moves the biological particles along the fluid flow path and to the interval between pulses of electrical energy “of amended claim 22;
- “computer configured to: a. control charging of the electrodes; and b. establish a flow rate of the fluid flow path in accordance with a sample processing rate” of new claim 34;
- “moving the cell suspension within the continuous flow system at a flow rate established by a computer-controllable pump to correspond to a sample processing rate” of new claim 38;
- “controlling individual thermoelectric cooling elements to cool portions of the continuous flow system” of new claim 42; and
- “automatically breaking an electrode prior to re-use” of new claim 44.

Accordingly, *all* the claims are patentable over Nicolau, and the current rejection should be withdrawn. Further arguments can be made about dependent claims, and Applicants reserve the right to do so, if necessary.

G. All the Claims Are Patentable Over Messerol I

Claims 25–26 and 28–29 stand rejected as being anticipated by U.S. Patent No. 6,090,617 (“Messerol I”). Applicants respectfully traverse.

Messerol I is not prior art. Each present claim (including new claims) claims priority to, and finds support in, U.S. Patent No. 5,720,921 (*see, e.g.*, cols. 25–26 and figures 14 and subsequent of the ‘921 patent). Thus, the claims have a filing date at least as early as March 10, 1995. Messerol I, on the other hand, has an effective filing date of December 5, 1996. Because Messerol I is not prior art, the present rejection should be withdrawn.

H. All the Claims Are Patentable Over Messerol II

Claims 14–15, 17–26, and 28–29 stand rejected as being anticipated by U.S. Patent No. 5,720,921 (“Messerol II”). Applicants respectfully traverse.

Messerol II is not prior art. Rather, Messerol II is a *parent* of the present application. *See* amended specification (explaining priority-tree of this application). Each present claim (including new claims) claims priority to, and finds support in, Messerol II. *See, e.g.*, cols. 25–26 and figures 14 and subsequent of Messerol II. Because Messerol II is not prior art, the present rejection should be withdrawn.

I. No Terminal Disclaimer is Needed

The Examiner has lodged double patenting rejections based on Messerol II. However, since Messerol II is a *parent* of the present application, no terminal disclaimer is required. The current application is already ensured not to extend beyond the life of Messerol II, given they are applications related by a claim of priority.

J. Conclusion

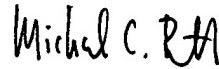
Applicants believe that this submission fully responds to all outstanding matters for this application. Applicants respectfully request that the rejections of all claims be withdrawn. All the claims are patentably distinct from the cited art.

Should the Examiner have any questions or desire to sustain any rejections, the courtesy of a telephone conference is respectfully requested so that all pending matters may be efficiently resolved.

Petition for Extension of Time

Pursuant to 37 C.F.R. § 1.136(a), Applicants petition for an extension of time of 3 months up to and including July 11, 2003, in which to respond to the outstanding Action. A check for the extension fee (\$465.00) is enclosed. Should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed materials, or should an overpayment be included, the Commissioner is authorized to deduct or credit fees to or from Fulbright & Jaworski Deposit Account No. 50-1212/MAXC:008USC1/MCB.

Respectfully submitted,



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Appendix A- Clean Set of Pending Claims

14. An apparatus for electroporation, comprising:
- a fluid flow path;
- electrodes disposed along sides of the fluid flow path and configured to subject biological particles moving along the fluid flow path to an electrical field suitable for electroporation; and
- a computer-controllable pump in fluid communication with the fluid flow path and configured to establish a flow rate of the fluid flow path in accordance with a sample processing rate.
15. The apparatus of Claim 14, wherein the electrical energy is pulsed.
18. The apparatus of Claim 14, wherein the electrodes comprise continuous band electrodes.
19. The apparatus of Claim 14, further comprising thermoelectric cooling elements in operative relation with the electrodes.
20. An apparatus for electroporation comprising:
- walls defining a fluid flow path;
- electrodes disposed along sides of the fluid flow path and configured to subject biological particles moving along the fluid flow path to an electrical field suitable for electroporation; and
- means for breaking the electrodes prior to the apparatus being removed from the support member whereby the apparatus cannot be re-used.;
21. The apparatus of Claim 20, wherein:
- the electrodes are wrapped around at least a portion of a spindle; and
- the means for breaking comprise spindles configured to rotate so as to stretch the electrodes beyond their tensile limits to break the electrodes and render them electrically inoperative.

22. An apparatus for electroporation comprising:
 - walls defining a fluid flow path;
 - electrodes disposed along sides of the fluid flow path and configured to subject biological particles moving along the fluid flow path to an electrical field suitable for electroporation;
 - a pump for moving the biological particles along the fluid flow path; and
 - a computer responsive to the rate at which the pump moves the biological particles along the fluid flow path and to the interval between pulses of electrical energy;
23. The apparatus of Claim 22, wherein the computer regulates the rate at which the pump moves the biological particles along the fluid flow path.
24. The apparatus of Claim 22, wherein the computer regulates the interval between pulses of electrical energy.
30. The apparatus of claim 30, the computer-controllable pump configured to vary the flow rate of the fluid flow path to match the sample processing rate.
31. The apparatus of claim 1, the sample processing rate corresponding to a processing rate of a centrifuge.
32. The apparatus of claim 1, the sample processing rate corresponding to an interval between pulses of electrical energy delivered to the electrodes.
33. The apparatus of claim 1, where one of the walls defining the fluid flow path is elastically deformable and at least another one of the walls defining the fluid flow path is substantially rigid.
34. An apparatus for electroporation, comprising:
 - a fluid flow path;

electrodes coupled to the fluid flow path and configured to subject biological particles moving along the fluid flow path to an electrical field suitable for electroporation; a pump configured to establish a flow rate of the fluid flow path; and a computer configured to:

- a. control charging of the electrodes; and
- b. establish a flow rate of the fluid flow path in accordance with a sample processing rate.

Claim 35 (new). The apparatus of claim 34, the sample processing rate corresponding to a processing rate of a centrifuge.

Claim 36 (new). The apparatus of claim 34, the sample processing rate corresponding to an interval between pulses of electrical energy delivered to the electrodes.

Claim 37 (new). The apparatus of claim 34, the computer configured to control the thermoelectric cooling elements individually to cool one location more or less than another location.

Claim 38 (new). The apparatus of claim 34, further comprising:

valves configured to control fluid flow;

thermoelectric cooling elements; and

wherein the computer is further configured to:

- c. control operation of the valves; or
- d. control the thermoelectric cooling elements.

Claim 39 (new). A method of incorporating a biologically-active substance into cells in a continuous flow system, comprising:

- a. introducing the cells into the continuous flow system;
- b. isolating the cells from at least some matter with which the cells are associated;
- c. mixing the cells with a biologically-active substance to provide a cell suspension;

- d. moving the cell suspension within the continuous flow system at a flow rate established by a computer-controllable pump to correspond to a sample processing rate;
- e. electroporating the cell suspension, thereby causing the biologically-active substance to be encapsulated in the cells; and
- f. incubating the cells to allow the cells to reseal to provide modified cells.

Claim 40 (new). The method of claim 38, further comprising:

- g. washing the modified cells to remove unencapsulated biologically-active substance therefrom.

Claim 41 (new). The method of claim 38, the sample processing rate corresponding to a processing rate of a centrifuge.

Claim 42 (new). The method of claim 38, the sample processing rate corresponding to an interval between pulses of electrical energy to the electrodes.

Claim 43 (new). A method of incorporating a biologically-active substance into cells in a continuous flow system, comprising:

- a. introducing the cells into the continuous flow system;
- b. isolating the cells from at least some matter with which the cells are associated;
- c. mixing the cells with a biologically-active substance to provide a cell suspension;
- d. electroporating the cell suspension, thereby causing the biologically-active substance to be encapsulated in the cells;
- e. controlling individual thermoelectric cooling elements to cool portions of the continuous flow system; and
- f. incubating the cells to allow the cells to reseal to provide modified cells.

Claim 44 (new). The method of claim 42, further comprising:

- g. washing the modified cells to remove unencapsulated biologically-active substance therefrom.

Claim 45 (new). A method for rendering an electroporation apparatus non-operational, the method comprising automatically breaking an electrode prior to re-use.

Claim 46 (new). The method of claim 44, the method comprising rotating a spindle to stretch an electrode wrapped around the spindle so as to break the electrode.